# Comparison of Non-Coding RNAs in Exosomes and Functional Efficacy of Human Embryonic Stem Cell- versus Induced Pluripotent Stem Cell-Derived Cardiomyocytes.

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**Public Summary:**
Both human embryonic stem cell-derived cardiomyocytes (ESC-CMs) and human induced pluripotent stem cell-derived CMs (iPSC-CMs) can serve as unlimited cell sources for cardiac regenerative therapy. However, the functional equivalency between human ESC-CMs and iPSC-CMs for cardiac regenerative therapy has not been demonstrated. Here, we performed a head-to-head comparison of ESC-CMs and iPSC-CMs in their ability to restore cardiac function in a rat myocardial infarction (MI) model as well as their exosomal secretome. Human ESCs and iPSCs were differentiated into CMs using small molecule inhibitors. Fluorescence-activated cell sorting analysis confirmed ~85% and ~83% of CMs differentiated from ESCs and iPSCs, respectively, were positive for cardiac troponin T. At a single-cell level, both cell types displayed similar calcium handling and electrophysiological properties, with gene expression comparable with the human fetal heart marked by striated sarcomeres. Sub-acute transplantation of ESC-CMs and iPSC-CMs into nude rats post-MI improved cardiac function, which was associated with increased expression of angiogenic genes in vitro following hypoxia. Profiling of exosomal microRNAs (miRs) and long non-coding RNAs (lncRNAs) revealed that both groups contain an identical repertoire of miRs and lncRNAs, including some that are known to be cardioprotective. We demonstrate that both ESC-CMs and iPSC-CMs can facilitate comparable cardiac repair. This is advantageous because unlike allogeneic ESC-CMs used in therapy, autologous iPSC-CMs could potentially avoid immune rejection when used for cardiac cell transplantation in the future. Stem Cells 2017.

**Scientific Abstract:**
Both human embryonic stem cell-derived cardiomyocytes (ESC-CMs) and human induced pluripotent stem cell-derived CMs (iPSC-CMs) can serve as unlimited cell sources for cardiac regenerative therapy. However, the functional equivalency between human ESC-CMs and iPSC-CMs for cardiac regenerative therapy has not been demonstrated. Here, we performed a head-to-head comparison of ESC-CMs and iPSC-CMs in their ability to restore cardiac function in a rat myocardial infarction (MI) model as well as their exosomal secretome. Human ESCs and iPSCs were differentiated into CMs using small molecule inhibitors. Fluorescence-activated cell sorting analysis confirmed approximately 85% and approximately 83% of CMs differentiated from ESCs and iPSCs, respectively, were positive for cardiac troponin T. At a single-cell level, both cell types displayed similar calcium handling and electrophysiological properties, with gene expression comparable with the human fetal heart marked by striated sarcomeres. Sub-acute transplantation of ESC-CMs and iPSC-CMs into nude rats post-MI improved cardiac function, which was associated with increased expression of angiogenic genes in vitro following hypoxia. Profiling of exosomal microRNAs (miRs) and long non-coding RNAs (lncRNAs) revealed that both groups contain an identical repertoire of miRs and lncRNAs, including some that are known to be cardioprotective. We demonstrate that both ESC-CMs and iPSC-CMs can facilitate comparable cardiac repair. This is advantageous because unlike allogeneic ESC-CMs used in therapy, autologous iPSC-CMs could potentially avoid immune rejection when used for cardiac cell transplantation in the future. Stem Cells 2017.